

Acne Treatment based on Selective Photothermolysis of Sebaceous Follicles with Topically Delivered Gold Plasmonic Particles

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ABSTRACT

Acne is a common dermatologic disease with major psychosocial impact as well as potential for scarring. Acne lesions originate from active sebaceous follicles and glands. Selective photothermolysis of the follicles is a potential therapy for long term remission. Our hypothesis was that light-absorbing microparticles could be delivered into sebaceous follicles, enabling local photothermal injury by optical pulses. A suspension of gold coated silica microparticles exhibiting plasmon resonance with strong absorption at 800 nm was topically applied to human pre-auricular and swine skin in vivo, and mechanical vibration was used to assist movement into the follicles. After exposure to 10-50 J cm⁻², 30 milliseconds, 800 nm diode laser pulses, microscopy revealed preferential thermal injury to sebaceous follicles and glands. Inflammation was mild; gold particles were not retained in swine skin 1 month after treatment, and uptake in other organs was negligible. An independent prospective randomized controlled clinical trials was performed for treatment of moderate to- severe facial acne. Clinically and statistically significant improvement of inflammatory acne was noted following three treatments given 1-2 weeks apart. Inflammatory lesions were significantly reduced at 12 weeks (p= 0.015) and 16 weeks (p =0.04) compared with sham treatments. This appears to be a well-tolerated, effective treatment for acne vulgaris.

Keywords: acne vulgaris, gold microparticles, selective photothermolysis, sebaceous follicles, clinical trial.

1. INTRODUCTION

Acne vulgaris can cause permanent facial scarring and negative psychosocial impact. The current therapies are either only mildly effective or have side effects. A much needed topical device based safe and effective treatment with no user compliance need has been developed. Anderson suggested that selective photothermolysis of sebaceous follicles could be achieved by introducing a light-absorbing chromophore into sebaceous follicles followed by exposure to optical pulses (Anderson, 1999). This method targets overactive sebaceous glands and infundbular hyperkeratinizing cells, the keys in acne pathophysiology. The infundibular opening and the infundibulum are a natural ingress to the sebaceous duct and gland for delivery of the chromophore, which was chosen to be inert plasmonic microparticles developed by Halas, *et al.* (1998). The microparticles are designed for strong near-infrared absorption. Particles with 120 nm diameter silica core, 15 nm thick gold shell were selected for peak absorption at 800 nm, a common hair removal wavelength. Further details are given by Paithankar, *et al.* (2015).

2. IN VIVO PORCINE STUDY

Treatment was performed on a live pig (IACUC approved study). Flank hair was epilated, particle suspension was massaged, and skin was treated with laser. Figure 1 illustrates an example of selective

photothermal damage to infundibulum and sebaceous glands in immediate post-treatment biopsy. Inflammation was mild and uptake in organs was negligible.

3. IN VIVO HUMAN HISTOLOGY

Seventeen subjects were enrolled in an IRB approved study of biopsies post treatment in post- or pre-auricular areas. Biopsies were analyzed via histology which showed local thermal injury to the infundibulum in 84% (27/32) and injury to sebaceous gland in 47% (15/32) of the specimens. No damage to adjacent dermis and epidermis was noted. Figure 2 is a collage of sebaceous follicles showing patterns of thermal damage to the infundibulum, sebaceous duct, and glands. Thus, selective photothermolysis was achieved.

4. ACNE HUMAN CLINICAL TRIAL

In a randomized clinical trial, subjects in the ‘active’ arm were treated three times, one week apart; mean laser radiant exposure was 33.4 J/cm². Subjects in the ‘sham’ arm were treated similarly but instead of the microparticles, vehicle was used with fluence of 10 J/cm². Fifty-one subjects (37 females) were enrolled with 27 in the active arm. At baseline, mean inflammatory lesion count was 44.8 and mean age 21.4 (range 16-26). Observations were done at baseline, 8, 12, and 16 weeks post baseline. Forty-nine of 51 subjects completed treatments and follow-up evaluations. Figure 3 shows the mean percent reduction from baseline in inflammatory lesion count at various time-points for the two arms. A statistically significant difference in reduction was noted at each point between the two arms. At 16-weeks post baseline, mean changes were -53% and -30% for active and sham, respectively (p=0.04). Figure 4 shows baseline and 12-week photographs of a subject in the active arm.

5. CONCLUSIONS

Laser treatment after follicular delivery of microparticles enables selective photothermolysis of sebaceous follicles and is a well-tolerated, safe, and effective treatment for acne vulgaris.

6. FIGURES

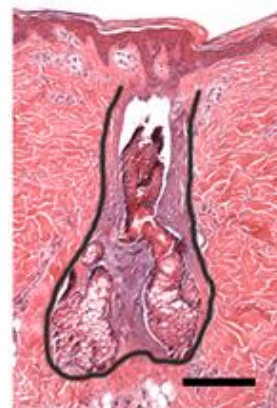


Figure 1. Histology with selective damage to follicle in in vivo pig skin, immediate post-treatment. Scale bar: 0.2 mm.

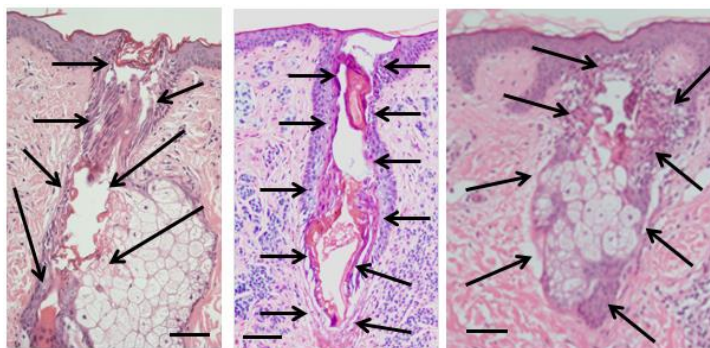


Figure 2. Histology of immediate post-treatment human biopsies showing thermal damage to the infundibulum and sebaceous gland. Back arrows: thermal damage. Scale bar: 0.1 mm.

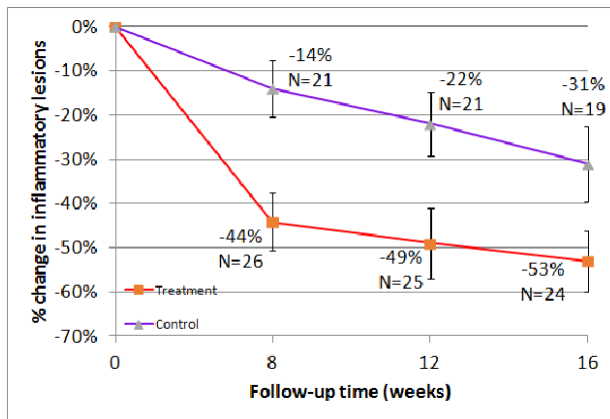


Figure 3. Mean percent reduction in inflammatory lesion count from baseline for treatment and sham arms. The bars represent the standard errors of the mean.



Figure 4. Baseline (top row) and 12-weeks post-baseline (bottom row) photos of a subject.

REFERENCES

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